REMARKS:

As the examiner can see, claims 1, 13 and 21 have been amended to state that the recombinant vesicular stomatitis virus (VSV) particle is live and replication competent, support for which may be found throughout the application as filed, for example at page 6, line 30 to page 7, line 1; page 12, lines 5-8; page 12, lines 21-22 and page 15, lines 1-14.

Claims 1-3, 5, 13-15, 17, 19-23, 25 and 27-31 were rejected under 35 USC 103(a) as unpatentable over Ito in view of Kahn and Vanderzanden.

The office action states that 'Ito teaches a recombinant VSV expressing Ebola glycoprotein. Kahn teaches a recombinant VSV expressing a major glycoprotein, and a method of eliciting an immune response with the recombinant VSV expressing a foreign glycoprotein. Vanderzanden teaches the Ebola surface glycoprotein is the most logical to use in a vaccine to induce antibodies and elicit an immune response.'

The office action further states that 'it would have been *prima facie* obvious to the person of ordinary skill in the art at the time the invention was made to prepare a vaccine comprising the glycoprotein of a hemorrhagic virus. The person of ordinary skill in the art would have been motivated to make use a VSV expressing the glycoprotein of a hemorrhagic virus to elicit an immune response because Ito teaches it is effective with Ebola (VHF), Kahn teaches how to prepare the composition and Vanderzanden suggests using the glycoprotein.'

Furthermore, the 'response to arguments' section states 'applicants argue "infectivity alone does not guarantee propagation and propagation does not

guarantee an immune response let alone vaccination". In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e. propagation) are not recited in the rejected claim(s).'

The 'response to arguments' section further states 'it would be easier if the G was not provided in trans therefore it would have been obvious to a person of skill in the art to try the method without providing the G in trans.'

As noted above, claims 1, 13 and 21 have been amended to state that the VSV particle is live and replication competent. Accordingly, it is noted that it is now recited in the claims that the VSV particle is capable of propagation, that is, is replication competent, that is, capable of self-replication.

As discussed in the previous responses and in the application as filed, for example at page 7, lines 8-10, 'it was believed that the GP of Ebola and Marburg were important virulence determinants and therefore disease symptoms were anticipated'. Accordingly, providing a live, propagating, recombination competent virus particle encoding an Ebola or Marburg or other VHF glycoprotein was considered to be risky and/or dangerous. However, as discussed in the previous responses, applicants were surprised to find that there were no associated side effects. As such while supplying in cis rather than in trans may have been considered easier, it was taught against by the prior art and therefore was not done out of concern for potential side effects.

In summary, the inventors have discovered that a VSVΔG particle can be constructed which has only a VHF glycoprotein and no VSV glycoprotein that can

be used safely as a vaccine based on its ability to propagate. This is in contrast with the prior art which teaches that VSV G must be supplied in trans and even then an immune response may not be elicited (Kahn) and that a propagating virus expressing one VHF glycoprotein (Zaire strain of Ebola) can cause symptoms associated with VHF and accordingly may not be safe. Ito teaches that Ebola GP can confer infectivity to a VSVΔG particle but as discussed above infectivity does not guarantee propagation, propagation does not guarantee an immune response and an immune response does not guarantee vaccination. Accordingly, the prior art taught that a VSVΔG-VHF G construct may not elicit an immune response even if VSV G was supplied in trans but such a construct could have considerable side effects. The inventors found surprisingly that neither was the case and that a safe and effective live, replication competent vaccine could be developed. Specifically, neither Ito nor Kahn teach or suggest a live, replication competent VSV particle encoding a VHF glycoprotein and for good reason – the prior art taught that such an infectious, propagating construct would induce symptoms associated with viral hemorrhagic fevers and accordingly could be dangerous.

In view of the foregoing, further and more favorable consideration is respectfully requested.

Respectfully submitted

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PER: _____

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